Allergy Abstracts

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Asthma and Hay Fever

Growth of Forty-Three Allergic Children During Cortisone Administration. Hill, L. W.: New England J. Med. **253**: 821, 1955.

Forty-three children, of whom 32 had asthma and 11 had eczema, received cortisone for periods varying from 3 to 30 months. The ages of these children ranged from 6 months to 12 years. Fifteen children were treated for more than 12 months. No child was given over 75 mg. of cortisone per day and only one received this dose for longer than 10 days. The usual maintenance dose varied between 25 and 50 mg. a day. Cortisone treatment was continuous and was given orally. Twenty-four children gained in height below the average rate, 15 above the average, and 4 at the average rate. In 417 months of cortisone treatment, 43 children grew in the aggregate of 80.75 inches. The average gain in the same number of months for 43 normal children of the same sex, age, and height would be 86.20 inches, a deficit of about 7 per cent for the cortisone-treated children. It was concluded that the retardation in growth in children taking moderate or small amounts of cortisone is not sufficient to warrant withholding the drug when it is needed. E. W.

The Seasonal Incidence of Atmospheric Mould Spores in Toronto (April 1953-April 1954). Fitzgerald, J. D. L., Fischer, J., and Doenne, A. E. M.: Canad. M. A. J. **72**: 700, 1955.

Petri dishes containing Littman agar were exposed for 12 minutes between noon and 2 P.M. daily on a window ledge four floors above the ground level. The spore colonies were identified 3 to 7 days later. Alternaria and Hormodendrum were most evident during the warm months between May and November. The highest counts were obtained after a rainfall or on hot, humid days. Occasional counts were also recorded during the winter after an unseasonable thaw. Aspergillus and Penicillium were present throughout the year, but only in very small quantities. Yeasts (rhodotorula and cryptococci) were found in large numbers throughout the year, especially during December, February, March, and April. Only a very small number of the other moulds were observed. These included Fusarium, Helminthosporium, Mucor, Phoma, Curvularia, Pullularia, Trichoderma, Montospora, Scopulariopsis, Stemphylium, Ghaetomium, Macrosporium, Papularia, Sporotrichum, and Geotrichum. R. W.

Chronic Ulcerative Colitis Due to Pollen Allergy With Six Case Reports. Rowe, A. H., Rowe, A. H., Jr., and Uyeyama, K.: Acta med. scandinav. **152**: 139, 1955.

Six cases of chronic ulcerative colitis which appeared to be related to the pollen seasons are presented. Skin reactions to pollen were not always positive. Exacerbations of the colitis could be produced by extremely minute doses of pollen extract. Clinical control by pollen extract injection was good, improving over a 2- or 3-year period. In some of the patients, foods and inhalants other than pollen were also important etiological factors. One patient had been controlled by pollen therapy alone for 14 years, except for a 2-week period about 8 months following cessation of therapy. E. K.

Hay Fever. Arnoldsson, H.: Nord. med. **54**: 1885, 1955.

Perennial specific hyposensitization treatment was given to 400 patients with hay fever for two or three years. After the optimum dose was attained, injections were given at 4-week intervals. Complete symptomatic relief was obtained in 34 per cent of the patients, and partial relief in 41 per cent. Of 82 patients treated with antihistamines alone, 60 obtained good results. There were 12 patients who were treated with cortisone because they had failed to respond both to hyposensitization therapy and to antihistamines. The dose of cortisone was 25 mg. three times daily initially, and then once daily throughout the pollen season. Improvement or complete relief was obtained in 10 patients and there were no side effects. It was concluded that specific hyposensitization is the treatment of choice since it may induce a permanent remission. M. C.

Radiotherapy of the Diencephalon in Asthma. Jacquelin, A., Lamy, R., Serra, R., and Gratay, A.: Semaine hôp. Paris **31**: 3972, 1955.

Among 247 patients with bronchial asthma who were treated by irradiation of the diencephalon, 48 per cent had complete remissions, 14 per cent showed improvement, and approximately 20 per cent obtained no relief. Poor results were observed in 18 per cent. Over a 2-year period, no exacerbation of symptoms occurred following this form of therapy. Analysis of the results indicated that many of the patients who responded favorably were severe, intractable asthmatics who had done poorly on other therapeutic regimens.

Remissions in these cases persisted for as long as 5 years. Radiotherapy of the diencephalon is indicated in those cases of asthma where a strong psychogenic component is present, where there is a marked eosinophilia, and in cases due to exogenous allergy. This type of therapy is not advised for patients with psychogenic asthma having unresolved conflicts, for patients with a strong localized bronchopulmonary component, or for patients with effort dyspnea. M. C.

Dermatology

Occurrence of Cataracts and Keratoconus With Atopic Dermatitis. Brunsting, L. A., Reed, W. B., and Bair, H. L.: Arch. Dermat. **72**: 237, 1955.

The records of 2,784 persons admitted to the Mayo Clinic between 1940 and 1953 for the treatment of atopic dermatitis, flexural eczema, or disseminated dermatitis were studied. Approximately 41 per cent of these individuals underwent slit-lamp examinations. Slit-lamp examination of 1,158 patients with atopic dermatitis revealed typical cataracts in 136 cases. In 79 instances, the cataracts were visible grossly or the patients knew of their visual impairment. There were 57 patients who had characteristic opacities, but no important visual impairment. The sex distribution was equal; the lesion was unilateral in 39 instances and bilateral in 97. The patients' ages ranged from 10 to 47 years, with symptoms of visual difficulty first becoming apparent in 21 patients during the first decade, in 38 during the second decade, in 13 during the third decade, and in 5 during the fourth decade. It was eventually necessary to perform cataract surgery on 34 patients.

The presence of dermatitis always antedated the development of cataracts, usually by several years. About 75 per cent of the patients had a history of infantile eczema and more than 50 per cent had either hay fever or asthma. A positive familial background of atopy could be elicited in about 60 per cent of the patients. Patients often noted rapid deterioration of vision associated with an exacerbation of the eruption, the loss of vision occurring in one or both eyes in a matter of weeks or a few months. In 3 patients, however, the loss was very gradual, taking from 3 to 10 years before the cataracts completely impaired their vision. Several patients who were followed for a period of many years had small opacities which remained the same and never progressed.

After reviewing the records of these patients with regard to any previous x-ray therapy which they may have had for their dermatitis, the authors concluded that there was no evidence that x-ray radiation was a factor in causing the cataracts.

Keratoconus was observed in 6 patients with atopic dermatitis, and 3 of these individuals were found to have minor lenticular opacities. R. W.

Hydrocortisone Ointment in the Treatment of Infantile Eczema. Hill, L. W.: New England J. Med. **252**: 1038, 1955.

Among 110 infants and children suffering from contact or atopic dermatitis who were treated with hydrocortisone ointment, 81 (73.6 per cent) had excellent results and 29 had poor results. One per cent ointment was found to be as effective as 2.5 per cent ointment. The author advises against the use of hydrocortisone ointment, with or without neomycin, when infection is present. Hydrocortisone ointment was found to be most efficient on superficial scaly or erythematous areas. Not only did it produce objective improvement, but it was effective in relieving pruritus. Recurrence was likely after treatment was discontinued. The chief disadvantage of this topical therapy

was found to be the expense involved in treating large areas. It is suggested that absorption of hydrocortisone is inevitable when large areas are treated; however, no systemic effects were observed. E. W.

The Role of Proteolytic Enzymes in the Production of Pruritus in Man. Arthur, R. P., and Shelley, W. B.: J. Invest. Dermat. **25**: 341, 1955.

Freshly prepared proteolytic enzymes were introduced into the normal skin of healthy adult males in an attempt to produce pruritus. With the single trichrome technique, by which practically an intra-epidermal injection can be given, erythema and wheal responses to the enzymes could be eliminated, making it possible to produce pruritus in the absence of visible changes in the skin. Each of 48 enzymes was tested on a minimum of 4 subjects. Pruritus occurred only with endopeptidases having a pH of 7 to 8. There were 6 such enzymes of plant origin and 4 of animal origin. The animal endopeptidases were chymotrypsin, trypsin, pancreatin, and plasmin. Since proteinases are present in epidermal cells and in blood, it was postulated that the release or activation of proteinases in the region of the superficial epidermal nerve network of receptors was an important factor in the clinical production of pruritus. It was possible to explain many divergent clinical states in which pruritus occurs through this mechanism. M. C.

Chlorpromazine Treatment for Relief of Itching in Severe Refractory Neurodermatitis. Tilley, R. F., and Barry, H., Jr.: New England J. Med. **252**: 229, 1955.

Chlorpromazine, in doses of 50 mg. three or four times daily, was administered to 3 patients with severe, intractable, generalized neurodermatitis of many years' duration. All previous medications, including cortisone in large doses, had proved unsuccessful. Following the use of chlorpromazine, there was prompt subjective and objective relief in the itching of these patients. One of these patients died of complications following a thrombosis of the femoral vein. Autopsy revealed an enlarged liver showing fatty degeneration. Since the patient had received no drugs for two weeks prior to death, it was considered improbable that the liver damage observed was due to chlorpromazine. A more likely cause was malnutrition. However, jaundice has occurred in a small percentage of patients who have received this drug. It was concluded that, in severe cases of neurodermatitis, chlorpromazine appears to be a timely addition to the therapeutic armamentarium, especially in cases where the intensity of the motor activity verges on the hypomanic. E. W.

Allergic Dermatitis Produced by Inhalant Molds. Jillson, O. F., and Adami, M.: Arch. Dermat. **72**: 411, 1955.

Mold plates were exposed for 12 minutes at 8 A.M. and at 5 P.M. every other day in Hanover, New Hampshire, during the period from October, 1952, through February, 1954. Following incubation at room temperature for one week the fungus colonies were identified and counted. The percentage incidence of the molds observed was as follows: yeasts (plus occasional bacteria), 26.3 per cent; Cladosporium (Hormodendrum), 21.7 per cent; *Mycelia sterilia*, 16.1 per cent; Pullularia, 11.5 per cent; Aspergillus, 5.0 per cent; Alternaria, 4.4 per cent; Oospora (Oidium), 4.1 per cent; Penicillium, 4.0 per cent; Phoma (Sphaeropsidales), 3.9 per cent. Another 3 per cent consisted of several sporadic fungi, especially Fusarium and Helminthosporium.

When snow completely covered the ground, there was a sharp drop in the mold count. Once there was a thaw, the mold count began to rise and continued to rise steadily until it reached its peak in the fall when the ground was covered by decaying leaves. The Aspergillus counts were quite constant throughout the year and Cladosporium and Pullularia were primarily responsible for the seasonal variations. The Alternaria counts were highest during the summer, but were much lower than counts taken elsewhere. The molds within a home often varied considerably from the mold content of the outside air. The predominant fungus in pillows and mattresses was Rhizopus.

The authors report the case of a 36-year-old housewife with a previous history of ragweed hay fever and infantile eczema who had had a recurrent dermatitis of the hands for 10 years. The rash was aggravated during the summer, spring, and fall and subsided during the winter. Patch tests were negative, but a skin test with ragweed gave a positive reaction and a skin test with 0.1 c.c. of 1,000 PNU mold extract showed a papular reaction at 48 hours. When the mold reaction was at its height, there was a simultaneous flare of the dermatitis. Mold and dust precautions were instituted and the patient was started on immunization therapy with mold extract and Staphylococcus ambotoxoid. After 2 months of treatment, she was considerably improved and, at the end of 9 months of therapy, she was asymptomatic and has continued to remain clear for the past 2 years.

The authors stress several factors which they regard as important in attempting to establish inhalant mold allergy as a cause of eczema; namely, the presence of an atopic background especially in the past personal history, seasonal incidence of the dermatitis consistent with the mold counts, a delayed papular reaction to the molds on skin testing, and a flare-up of the dermatitis coincident with the positive papular reaction. R. W.

Prednisolone Topically and Systemically. A Clinical Evaluation in Selected Dermatoses: Preliminary Report. Frank, L., and Stritzler, C.: Arch. Dermat. **72**: 547, 1955.

The authors studied the comparative effectiveness of the topical application of 0.25 per cent and 0.5 per cent prednisolone ointment and of 1 per cent hydrocortisone in an identical base, using contralateral areas wherever possible for comparison. Two hundred fifty-six patients with dermatoses expected to be responsive to hormone therapy were chosen for this study. If no contralateral areas were available, then one medication was alternated with the other to evaluate the efficacy of the two medications. The writers also treated 67 patients with oral prednisolone. Patients were given 25 to 40 mg. of prednisolone initially and then maintained on a dose of 15 to 20 mg. daily. Twenty-one of these patients had been on oral hydrocortisone before being changed to prednisolone, and were given 5 mg. of prednisolone for each 20 mg. of hydrocortisone they previously had taken. None of the patients were put on dietary or sodium restrictions.

Hydrocortisone was found to be definitely more effective than prednisolone topically. Prednisolone was beneficial topically only in conditions responsive to hydrocortisone, but response to prednisolone was not so rapid as that obtained to hydrocortisone. In several patients, prednisolone produced an irritation and had to be discontinued, but reactions to patch tests wih prednisolone on these individuals were negative. The 0.25 per cent and the 0.5 per cent concentrations of prednisolone were equally effective when applied topically.

When given by mouth, prednisolone was a highly effective drug in relieving various types of pruritic or inflammatory dermatologic conditions. Several patients who had not been controlled on 80 to 100 mg. of hydrocortisone

did well on 15 mg. of prednisolone daily. Side effects to oral prednisolone were minimal. Many patients had a sense of well-being and increased appetite, while a few complained of abdominal distress or moon face. None of the patients developed gastrointestinal lesions. It was necessary, however, to discontinue the medication in 2 individuals; one of these patients developed severe heartburn and the other developed a severe depression. No hypertension, sudden weight gain, edema, or glycosuria were observed. Milligram for milligram, oral prednisolone was found to be approximately four times as effective as oral hydrocortisone. The authors stress the fact that most patients can tolerate prednisolone on a normal unrestricted diet without the complications of hypertension and sodium and fluid retention. R. W.

Otorhinology and Ophthalmology

Effects of Tyzine and Other Vasoconstrictors on Ciliated Epithelium. Hutcheon, D. E., and Cullen, M. R.: Arch. Otolaryng. **62**: 154, 1955.

The effect of several vasoconstrictors on ciliary movement of rat tracheal epithelium was studied to compare their relative local toxic properties. Tracheal rings, immersed in Locke-Ringer's solution, at pH 7.2, were exposed to varying concentrations of naphazoline, tetrahydrozoline (Tyzine), ephedrine, and phenylephrine. The percentage of rings in which ciliary movement was stopped after 15 minutes of exposure to the drugs was plotted against the logarithm of the concentrations of the vasoconstrictors. Naphazoline arrested ciliary movement in the lowest concentrations, tetrahydrozoline and ephedrine at intermediate concentrations, and phenylephrine in the highest concentrations. The concentrations necessary to suppress ciliary motility in 50 per cent of the rings were 0.4 per cent for naphazoline, 1.3 per cent for tetrahydrozoline, 2.4 per cent for ephedrine, and 4.2 per cent for phenylephrine. These figures, when divided by the therapeutic concentrations of these nasal decongestants, resulted in the following therapeutic indices: 2.4 for ephedrine, 4.0 for naphazoline, 12.0 for tetrahydrozoline, and 17.2 for phenylephrine. The effect of tetrahydrozoline on ciliary activity was studied in various pH zones. There was less depression of ciliary movement in acid media than in neutral or alkaline media. In microscopic studies of epithelia in which ciliary movements were arrested by vasoconstrictors, globoid bodies were seen to extrude from the epithelial cells. These bodies appeared to be cytoplasmic in nature. This effect was felt to be a physicochemical effect of the drugs on the cell surface. B. S.

Hydrocortisone in Treatment of Allergic Conjunctivitis, Allergic Rhinitis, and Bronchial Asthma. Foulds, W. S., Greaves, D. P., Herxheimer, H., and Kingdom, L. G.: Lancet **1**: 234, 1955.

Hydrocortisone in a 2.5 per cent concentration was instilled locally into the eyes of four patients suffering from extremely severe perennial allergic conjunctivitis. Each of the patients obtained excellent results, two of them being asymptomatic 7 to 21 days after receiving two drops three times daily for two days. Fifteen patients suffering from perennial allergic rhinitis were treated by nasal inhalation of 15 mg. of hydrocortisone daily. Eleven of the 15 patients were subjectively and objectively improved. A control period was obtained by interrupting therapy for a couple of weeks or by substituting an inert powder for the hydrocortisone. Of the four patients who failed to respond well, one found the powder very irritating, one developed urticaria from it, and one patient did not employ it regularly.

Inhalations of hydrocortisone with a particle size under 5 microns were tried in 15 patients with intractable asthma. Each was given 15 mg. daily for several weeks, and then the cartridges containing an inert powder were substituted for the hydrocortisone. Twelve of the asthmatic patients obtained definite improvement while three patients were not helped. When a placebo was substituted, the beneficial effects were quickly dissipated. Increasing the dose above 15 mg. per day failed to produce more beneficial results. The authors are confident that local hydrocortisone therapy is of therapeutic value in the treatment of allergic conjunctivitis, allergic rhinitis, and bronchial asthma; they point out the advantages of avoiding the dangerous side reactions associated with systemic steroid therapy. R. W.

Miscellaneous Allergies

Hypersensitivity Angiitis. Edge, J. R., Fazlullah, S., and Ward, J.: Lancet **1**: 1153, 1955.

The case of a 33-year-old woman who developed a mild serum-sickness-like reaction following the administration of penicillin for an acute otitis media is reported. During the following few days, she complained of pleuritic pain. Shortly thereafter two dense, homogeneous, rounded opacities in the lower portion of the right lung were found on x-ray. When she developed a pleural effusion, she was hospitalized for further study. Although the diagnostic tests were negative, she was empirically put on an antituberculous regime and given 1 Gm. of streptomycin and 200 mg. of isoniazid daily. One week later, she developed a rash and a fever similar to that which had occurred following penicillin therapy. The streptomycin was discontinued and promethazine (Phenergan) was given. Two days later, after the isoniazid had also been discontinued, the temperature dropped from 104° to 100° F. During the next week, the rash cleared, but the patient developed acute urinary retention. She also showed mild neurological symptoms for several days, but appeared to be making satisfactory progress and was finally free of symptoms.

About one week later, the patient was given a test dose of 1 Gm. of streptomycin intramuscularly, which was followed by a mild serum-sickness-like reaction. When a test dose of 20 mg. of isoniazid was given 3 days later, the patient soon developed a fever and a severe bilateral conjunctivitis. The eye condition progressed to such an extent that it simulated phlyctenular conjunctivitis. A Mantoux test with a 1-1,000 dilution of O.T. gave a negative reaction. The patient also developed numerous joint symptoms and was given 100 mg. of ACTH daily. Her temperature quickly dropped to normal and the dosage of ACTH was gradually reduced during the next 4 days. At this time, she suffered a relapse and cortisone, 25 mg. every 6 hours orally, was substituted for the ACTH. During the next few days, she was found to have a blood urea of 300 mg. per 100 ml. She showed signs of pulmonary edema and deteriorated rapidly.

At post-mortem, the small arteries of the heart, spleen, lungs, and portal tracts indicated an arteritis. None of the larger vessels showed arteritis. The kidneys showed numerous areas of fibrinoid necrosis in the glomerular tufts with hyaline and leukocytic casts present in many of the tubules. Several areas of necrosis were found in each adrenal cortex but no definite arteritis was present within the gland substance.

The authors suggest that the reaction to penicillin initiated the fatal chain of events. They further imply that subsequent drug reactions may have hastened the outcome. Because of the severe nephrotoxic reaction, it is inferred that the cortisone therapy also may have been a factor in causing the diffuse arteritis. R. W.

Jaundice Following the Administration of 50 Mg. of Chlorpromazine. Sussman, R. M., and Sumner, P.: New England J. Med. **253**: 499, 1955.

A 53-year-old woman developed painless, obstructive jaundice and pruritus two days after the ingestion of 50 mg. of chlorpromazine. Hyperbilirubinemia, bilirubinuria, elevation of the alkaline phosphatase with a normal cephalin flocculation and cholesterol esterification were found on chemical investigation. A gall bladder series performed after the subsidence of the jaundice was essentially normal. Ingestion of chlorpromazine some time later precipitated the same clinical picture in milder form with essentially the same laboratory findings. The temporal relation between ingestion of the drug and the appearance of jaundice is suggestive of hypersensitivity. Furthermore, "the short interval between the administration of the drug and the appearance of pruritus as a symptom of jaundice two days thereafter is consistent with the concept of an accelerated reaction due to previous sensitization by a drug sufficiently related to chlorpromazine immunochemically to produce so-called cross-sensitization." It was pointed out that there is a close chemical relationship between chlorpromazine, a known urticariogenic substance, and Phenergan, a widely used antihistaminic. E. W.

Anaphylactic Reaction Following the Oral Administration of Penicillin. Lang, L. P., and Clagett, H.: New England J. Med. **253**: 652, 1955.

A severe constitutional reaction accompanied by shock occurred in a 53-year-old woman following the ingestion of one tablet of penicillin containing 200,000 units. Within a minute, she felt numbness and tingling of her lips, which became swollen; then she lost consciousness and fell to the floor. Shortly thereafter she was found conscious, but with a barely palpable pulse. Examination at this time showed marked cyanosis of the lips and nail beds, a generalized erythematous blush involving the whole body except the face, and edema of the tongue, lips, and hands. There was no respiratory obstruction. The temperature was 101° F.; the blood pressure was 85/55. The laboratory findings were negative except for 0 to 2 granular casts per high-power field in the urinary sediment. An electrocardiogram showed flattening of the T-waves, with prolongation of the QT interval suggesting an electrolyte imbalance. The patient was given levarterenol bitartrate, 4 mg. per liter of physiologic saline solution intravenously, and 125 mg. of cortisone intramuscularly. For the first 9 hours levarterenol had to be given continuously in order to maintain the blood pressure at a normal level. Nine hours after admission the patient appeared to have recovered. On further questioning, it was found that she was atopic, but she had had no previous reactions to penicillin following its administration by either the intramuscular or the oral route. No skin tests with penicillin were done. The dangers associated with penicillin therapy in patients with known allergic disease are emphasized. E. W.

Schönlein-Henoch's Purpura. Three Cases With Fish or Penicillin as Antigen. Jensen, B.: Acta med. scandinav. **152**: 61, 1955.

Three cases of Schönlein-Henoch's purpura are described. In one 6-year-old boy, angioedema was also present. Scratch tests performed on him with fish and shrimp were positive. The elimination of these foods was followed by clearing of the condition over a period of weeks. In another 4-year-old boy, scratch tests gave positive reactions to several fungi but not to fish. On being fed fish, however, he developed purpura. Fish was avoided and he remained well for a period of time. The third patient, a man aged 27 years,

had been given 3 penicillin injections. A few days later he developed joint pains, abdominal pain, and bloody stools. He was adjudged sensitive to penicillin on the basis of a positive skin reaction which appeared within 15 minutes after an intracutaneous test with a solution of penicillin. All three cases failed to show abnormal blood platelet counts. E. K.

Anaphylaxis

Tissue Reactions to Anaphylactic and Anaphylactoid Stimuli: Proteolysis and Release of Histamine and Heparin. Ungar, G., and Damgaard, E.: J. Exper. Med. **101**: 1, 1955.

Guinea pigs were sensitized to egg albumin or rabbit serum and then sacrificed by exsanguination. Lung and liver slices were prepared, dried, and suspended in buffered saline. Lung perfusions were also carried out. The addition of specific antigen or an anaphylactoid agent such as Tween 20, fibrinolysin, morphine, or octadecylamine to sensitized tissue resulted in increased histamine release, heparin release (even from lung tissue), and proteolysis. Protein breakdown in the liver occurs without an associated histamine release. When histamine was added to tissue slices no proteolytic reaction resulted and no additional histamine was released from the tissue. When proteolysis was inhibited by the addition of sodium salicylate, polylysine, or soybean trypsin inhibitor, histamine release, heparin release, and protein hydrolysis were all markedly decreased. Sensitized lung perfused with antigen showed a sudden marked increase in histamine release and in protein destruction when normal guinea pig serum was added to the perfusate. Protease activity was elicited from extracts of tissue homogenates treated with antigens and anaphylactoid agents. Enzyme extraction of these homogenates resulted in lowered protease activity. When antigen or anaphylactoid agents were added to tissue extracts which were free of cell debris, enzymatic activity fell to very low levels except when streptokinase was the activator.

It is suggested that the anaphylactic or anaphylactoid reaction causes either serum or tissue kinase to activate an inactive precursor in the tissues to become a protease. This then produces proteolysis. Histamine and heparin release may then be the consequence of tissue protein destruction. E. K.

Antibody Production in Balb/c Mice Following Injection of Lyophilized Tumor S621 in Freund's Adjuvant. Fink, M. A., Smith, P., and Rothlauf, M. V.: Proc. Soc. Exper. Biol. & Med. **90**: 590, 1955.

Mice immunized with lyophilized homologous tumors possess the ability to cause a regression of a viable implant of the tumor. In such mice, anaphylactic shock was demonstrated on a second intravenous injection of the antigen. The authors now report on antibody studies, by three different techniques, in mice (strain BALB/c) immunized with lyophilized homologous tumor (S621) in Freund's adjuvant. These animals were shown to have a much greater protection (over 50 per cent) than those treated without Freund's adjuvant. The uteri of these mice were demonstrated to be anaphylactically sensitive to the tumor antigen by the Schultz-Dale technique. Peritoneal exudate cells from mice in this series were lysed in the presence of antigen and complement, a phenomenon which could not be demonstrated with normal lyophilized mouse liver as antigen.

Despite such evidence of antibody production in these animals, no circulating antibodies to tumor S621 have been demonstrated as yet by any of the usual serum tests, including precipitation, complement fixation, and passive protection with serum from immunized mice. B. S.

Fall in Rectal Temperature as an Indication of Anaphylactic Shock in the Mouse. Kind, L. S.: J. Immunol. **74**: 387, 1955.

White mice were inoculated intraperitoneally with *H. pertussis* vaccine or horse serum or with a mixture of both antigens. Eight days later, the animals were placed for 2 days in a room thermostatically controlled at 21° C. During this period of acclimatization, rectal temperature measurements were made. The animals were then injected intraperitoneally with 0.1 ml. of a 1:20 dilution of horse serum. Rectal temperatures were recorded one-half, 2, and 8 hours after this challenge dose. Several nonsensitized control mice were also injected with varying quantities of undiluted horse serum. Of the 31 mice inoculated with pertussis vaccine plus horse serum, 6 died in anaphylactic shock. The remaining animals, with few exceptions, showed evidence of mild anaphylaxis and a fall in rectal temperature of 2° C. or more. The average rectal temperature dropped sharply during the first 30 minutes, became lower in the next hour and one-half, and returned toward the normal value in 8 hours. Several animals without evidence of anaphylaxis showed a fall in rectal temperature. The control animals failed to demonstrate this fall in temperature after the challenge injection of horse serum, even when much larger doses were given. These studies indicate that a fall in rectal temperature is a consistent finding in horse-serum-sensitized mice undergoing anaphylactic shock and can be employed as an accurate index of sensitivity in experimental studies. B. S.

Effects of Corticotropin and 11-Desoxycorticosterone on Anaphylaxis and Tissue Electrolytes in Mice. Einbinder, J. M:, Fox, C. L., Jr., and Nelson, C. T.: Am. J. Physiol. **182**: 518, 1955.

Previous studies have shown that the administration of cortisone to mice produces a definite change in tissue electrolytes characterized chiefly by a decrease in the potassium content of the tissues. In anaphylactic shock, the potassium content of the tissues is significantly increased. Mice treated with cortisone can be protected from fatal anaphylaxis. The present studies showed that ACTH produces some decrease in the potassium of the tissues but does not provide appreciable protection against anaphylaxis. Mice treated with ACTH and subsequently shocked anaphylactically showed the same electrolytic changes which take place in untreated shocked animals. DCA, when administered to mice, produces a significant increase in tissue sodium, a slight decrease in tissue potassium, and a marked increase in the vulnerability of the animals to anaphylactic shock. With the change in the potassium content of the tissues, the sodium content is affected in reverse order, particularly in the muscles and viscera. A reduction in plasma volume occurred concomitantly with these electrolyte changes. H. F.

Pharmacology, Physiology, and Pathology

Clinical Value of a Tracing of Forced Expiration (Expirogram). I. Pulmonary Disease. Franklin, W., Michelson, A. L., Lowell, F. C., and Schiller, I. W.: New England J. Med. **253**: 799, 1955.

The kymographic tracing made on a rapidly moving kymograph during the performance of vital capacity tests is presented as a valuable test of pulmonary function in the management of patients with respiratory disease. The tracings were made with a spirometer of 6-liter capacity having a diameter of 16 cm.

and recording on an adjustable-speed kymograph run at 0.56 cm. per second. Normal adult subjects expelled a volume of 70 to 85 per cent of the vital capacity in the first second; children expelled more than 85 per cent in the first second; whereas elderly subjects with no evidence of pulmonary disease expelled as little as 70 per cent in the first second. In the absence of pulmonary disease, no change in rate of expiration or vital capacity was noted after the administration of a bronchodilator drug. Experience with the expirogram revealed marked changes in the tracings in different pulmonary diseases. Expirograms and case histories were used to illustrate the efficacy of therapy and the course of the disease in patients with bronchial asthma, pulmonary emphysema, senile emphysema, and pulmonary fibrosis. In most cases, it was shown that the expirogram served as a better guide to therapy and to the course of disease than did x-ray, clinical, or subjective improvement. E. W.

Acute Vascular (Schönlein-Henoch) Purpura—an Immunologic Disease? Kreidberg, M. B., Dameshek, W., and Latoraca, R.: New England J. Med. **253**: 1014, 1955.

Acute vascular (Schönlein-Henoch) purpura was observed in 15 children whose ages varied from 2 to 10 years. There were 9 girls and 6 boys in this group. In all except one of the cases in which pyuria was present, there was a history of antecedent infection of the pharynx or tonsils, followed by a period of from 3 to 28 days before the appearance of purpuric spots. In 7 patients, the skin lesions began as itching urticarial wheals which became purpuric within a short time. Joint symptoms, varying from slight aching in a single joint to painful swelling of many joints, occurred in 14 of the patients. There were gastrointestinal symptoms in 8 cases, or 53 per cent. The patients complained of severe colicky abdominal pain, and in 6 patients there was a history of melena for a period of from 4 to 9 days. Bright red blood was not seen in the stools of any patients in this series. Three patients showed the features of acute nephritis, including hematuria and albuminuria. In one, the symptoms and signs of nephritis appeared 49 days before the onset of the purpuric eruption. Evidence of microscopic hematuria persisted for 4 months in the first case and for 15 months in the second. In the third patient, when seen 30 months after the onset, urinalysis revealed no albuminuria or gross hematuria, but an Addis count showed 1,850,000 red blood cells and 411,100 white blood cells per cubic millimeter. These findings indicated that renal lesions are the slowest to heal and that nephritis in association with purpura may have a graver prognosis than when it occurs alone. Red cell counts in this series varied between 3,100,000 and 4,500,000, and the white cell count between 6,900 and 19,000. Thirty-three per cent of the patients had eosinophilia, with counts ranging from 5 to 11 per cent. The patient with 11 per cent blood eosinophilia also had eosinophilia of the bone marrow. The platelet counts, bleeding time, clot retraction, coagulation time, prothrombin time, and prothrombin consumption were normal in all cases. Only 3 patients in this series gave a positive history of allergic disease, such as asthma, hay fever, or eczema. One of these patients had had asthma and a history of a sensitivity reaction to sulfonamide; in another, penicillin sensitivity had developed at the age of 2½ years. Skin biopsies in 4 patients indicated an acute inflammatory reaction involving the capillaries in which a cuff, consisting of polymorphonuclear leukocytes, lymphocytes, histiocytes, edema, and eosinophils in small numbers, was found. There was swelling of the endothelial cells. Edematous thickening of the capillary wall was found. About many of the lesions, there was an

extravasation of erythrocytes into the surrounding tissue. The lesions, although found in all areas of the skin, were most frequently located in the superficial corium. In the most severe cases, the small arterioles were also surrounded by this inflammatory exudate. Important negative findings were the absence of necrosis or changes in the collagen fibers, absence of fibrin in the inflammatory lesion, absence of thrombi in the capillaries, and absence of necrosis of the vessel walls. When an active focus of infection was found, treatment with the appropriate antibiotic was instituted. ACTH was used in only 3 patients, in whom no improvement had occurred with conservative measures. Within a week after ACTH therapy was instituted, purpuric lesions had disappeared. It was suggested that "the latent period between remission of the infection and the appearance of purpura may be the time during which, in response to an antigenic stimulus of unknown nature, an immunologic mechanism develops. An immunologic storm, with an antigen-antibody reaction at the end organ (small blood vessels), probably determines the picture of acute inflammatory perivasculitis found in the walls of the small blood vessels of the corium, capillaries of the synovia, glomeruli of the kidneys and small blood vessels of the walls of the intestines and in turn explains the varied symptomatology." E. W.

Plasma Penicillin Levels From Oral Penicillin V and G and Intramuscular Penicillin G. Nichols, R. L., Jones, F. R., Jr., and Finland, M.: Proc. Soc. Exper. Biol. & Med. **90**: 688, 1955.

The authors compared the plasma levels of penicillin produced by the same amounts of penicillins V and G, administered orally or intramuscularly at various dosage levels. The three dosage forms included (1) the free acid of penicillin V in 200,000 unit tablets, (2) buffered potassium penicillin G ("Pentids," Squibb) in 200,000 unit tablets, and (3) aqueous potassium penicillin G intramuscularly. The dosage levels were 200,000 units, 400,000 units, and 1,000,000 units. The interval between doses was at least 48 hours. The time of administration was one-half hour after breakfast. The penicillin assays in the plasma were determined by the twofold broth dilution method employed in previous studies. The assay organism was Strep. 98 and comparisons were made with a penicillin G standard solution. Blood samples were procured before and 1, 2, 4, and 6 hours after each dose.

At each of the three dosage levels, oral penicillin V produced higher and more sustained plasma levels of penicillin activity than did oral penicillin G. At the 200,000 level an intramuscular dose of penicillin G produced earlier and higher, but less sustained, peak levels than did penicillin V taken orally. The total amount of penicillin absorbed with these two forms of administration was the same. However, at the 400,000 and 1,000,000 unit levels, intramuscular penicillin G produced higher and more sustained blood levels than did oral penicillin V. Although subjects over 60 years of age were slower than the average in obtaining peak levels, they tended to manifest higher and more sustained levels than did younger subjects. B. S.

Pituitary ACTH Content of Thyroidectomized-Stressed Rats. Hess, M., Slade, I. H., Ammons, J. C., and Hendrix, V.: Am. J. Physiol. **183**: 261, 1955.

The adrenals of stressed-thryoidectomized rats appear to be more sensitive to ACTH stimulation than those of stressed-intact animals. This was demonstrated by a significantly greater depletion of the adrenal ascorbic acid in the

former than in the latter group of animals. This loss of adrenal ascorbic acid occurred in spite of the fact that the ACTH content of the pituitary glands of the stressed-thyroidectomized rats was shown to be no greater than that of stressed-intact rats. H. F.

Blood Histamine in Patients With Eosinophilia. Achari and Acharya: Patna J. Med. **29**: 595, 1955.

The blood histamine content of normal adults was compared with that of patients showing varying degrees of eosinophilia. A total count of 250 to 750 eosinophiles per cubic millimeter was regarded as normal. The blood histamine values for the normal group ranged between 0.015 and 0.031 meg. per cubic centimeter, while in patients with eosinophilia the values were 0.025 to 0.052 meg. per cubic centimeter. There was no correlation between the degree of eosinophilia and the increase in histamine content of the blood. The increased histamine content of the blood in eosinophilia was considered significant. M. C.

Miscellaneous

Hypersensitivity in Mice With Experimental Histoplasmosis. Salvin, S. B.: J. Immunol. **75**: 1, 1955.

When white mice were injected intraperitoneally with 10^9 live cells of the yeast phase of *Histoplasma capsulatum* suspended in 5 per cent mucin, 86 per cent of the animals died within 21 days after inoculation. Most of these animals died during the fourth to tenth days postinjection. The type of mortality differed significantly when the primary intraperitoneal injection, consisting of 10^6 live cells, was followed in 14 days by a secondary intraperitoneal injection of 10^9 cells in 5 per cent mucin. Sixty-one per cent of the animals died within 21 days after the secondary injection and 90 per cent of these animals succumbed during the first 48 hours after the challenge. When the secondary challenge injection consisted of 5 per cent mucin alone, none of the animals died within the first 48 hours. These studies suggested that the previous sublethal intraperitoneal injection induced the development of a hypersensitive state, manifest within 48 hours after challenge.

Studies were then undertaken to clarify the various determining factors responsible for the induction of the hypersensitive state. It was found that the route of administration of the primary sensitizing inoculation was not a significant factor, although the intracerebral and intraperitoneal routes were most effective in inducing the hypersensitive state. In general, the larger the primary dose of live yeast cells, the greater was the number of mice that died within 48 hours after the challenge dose given 14 days later. The initial studies were repeated with variations in the interval between the primary and secondary injections. When the interval was 2 to 4 hours, the animals neither died within 48 hours after the secondary injection nor showed increased resistance to subsequent challenge. With a 48-hour interval, resistance to reinfection began to appear. The optimal interval for induction of resistance was 5 to 7 days. Evidence of hypersensitivity appeared after a 9-day interval and this response reached its maximum at a 14-day interval. Both increased resistance to reinfection and hypersensitivity persisted for at least 35 days after the primary infection. When the dose of the primary injection was increased, the interval required to produce a state of hypersensitivity was reduced to 4 to 5 days. When the primary injection was made with several species of pathogenic fungi other than *H. capsulatum* and the challenge injection was made with *H. capsulatum*, no evidence of hypersensitivity was noted. In other experiments,

dead acetone-dried yeast cells of *H. capsulatum* were substituted for viable cells in the primary injection. Under these circumstances, a state of hypersensitivity could not be induced. However, when viable cells were employed in the primary injection, the subsequent injection of dead cells appeared to provide sufficient antigenic stimulation to cause death within 48 hours. Pathologic studies on the animals in this experiment and on control animals revealed no significant difference in the numbers of viable fungal cells in the spleen, liver, and kidney, indicating that death after the administration of dead cells was not due to a sudden dissemination of *H. capsulatum*.

Although the existence of a hypersensitive state in histoplasmosis has long been known, these studies are the first which indicate that hypersensitivity may actually produce such a severe systemic condition in animals with histoplasmosis that death can result. This knowledge may be clinically important in relation to the use of a chemotherapeutic agent which would cause the sudden destruction of large numbers of *H. capsulatum* and the liberation and absorption of their proteins or endotoxins. B. S.

Eosinophil Response to Toxoids in Actively and Passively Immunized Mice. Spiers, R. S., and Wenck, U.: Proc. Soc. Exper. Biol. & Med. **90**: 571, 1955.

Mice were immunized to diphtheria toxoid by a series of 5 subcutaneous injections administered in 13 days. Immunization to tetanus toxoid was produced similarly with fluid toxoid in one series, and in another series with alum phosphate precipitated toxoid followed by fluid toxoid in a series of 4 injections lasting 29 days. In all cases, the challenging injection of toxoid was given intraperitoneally 7 days after the last immunizing injection. Passive immunization was produced by an injection of tetanus antitoxin 1 or 72 hours prior to the injection of fluid tetanus toxoid.

Four days after the challenging intraperitoneal injection of toxoid, the eosinophil content of the peritoneal exudates was studied. Nonimmunized animals showed few eosinophils in comparison to immunized ones in which there was as much as a 50-fold increase. The passively immunized mice failed to show a similar increase.

The challenging injections also produced increases of mononuclear cells in the actively immunized animals but not to the same degree as the eosinophils. The eosinophil excess in the peritoneal fluid persisted for as long as 10 days. The evidence suggests that the eosinophils are related to antibody production. Treatment with cortisone and x-ray which tend to inhibit antibody production also tends to prevent eosinophil accumulation in the peritoneal fluid. B. S.

Delayed Blood Coagulation in Rabbits With Localized Shwartzman Reaction. Volk, B. W., and Losner, S.: Proc. Soc. Exper. Biol. & Med. **90**: 618, 1955.

Experiments performed on rabbits revealed that there is a prolongation of the Lee-White clotting time when a localized Shwartzman reaction is induced in these animals. Blood samples were obtained through cardiac puncture at various stages of the reaction. Twenty-four hours after the provocative intravenous injection when the local reaction had become pronounced, the Lee-White clotting time was 18 minutes. The next day it fell to 8.3 minutes and 4 days later to 4.3 minutes. The normal reading in untreated rabbits is 5.5 minutes. The prothrombin times in the experimental animals were not affected during the period when the Lee-White clotting time was altered. Hence, rabbit blood, which normally shows a high degree of hypercoagulability, tends to lose this property on the appearance of a localized Shwartzman reaction. B.

Influence of Cortisone on Experimental Viral Injection. II. Effects on Antibody Formation and Acquired Immunity. Kilbourne, E. D.: Proc. Soc. Exper. Biol. & Med. **90**: 685, 1955.

The ability of cortisone to inhibit antibody formation in mice during the course of active infection with influenza A viruses is reported in this study. The two avirulent virus strains which were used were capable of inducing high antibody titers without causing pneumonia or death.

Neutralizing and hemagglutination-inhibiting antibodies were suppressed following prolonged administration of cortisone initiated on the day of injection. Large doses given only at the onset of infection failed to produce these results.

In another series of experiments, mice previously immunized by intranasal inoculation with avirulent influenza A virus were challenged, after 2 weeks, with a virulent strain. In some animals, cortisone was injected in large doses at the time of the challenging inoculation.

In the latter animals, pulmonary lesions involving at least 33 per cent of the total lung volume usually developed and the virus was demonstrable in the lungs 7 days after the challenge. These changes were not observed in the immunized animals which received no cortisone. Thus, large single doses of cortisone, although not sufficient to suppress antibody formation, diminished the acquired immunity in mice and promoted the development of pulmonary pathology and persistence of pulmonary virus. B. S.

Thrombocytopenic Purpura Associated With Oxytetracycline Therapy. Beckett, A. G., and Foxell, A. W. H.: Lancet **1**: 1053, 1955.

A 77-year-old man with extensive bilateral pneumonia was given penicillin and sulfadiazine therapy. When he failed to improve within 24 hours, the therapy was changed to oxytetracycline. He developed acute heart failure 6 days later, the dose of oxytetracycline was raised, and he was maintained on this for 6 days until clinical improvement warranted reduction of the dose. Three days after the oxytetracycline was discontinued, the patient showed signs of severe purpura with bleeding from numerous sites in the body. As the hemorrhagic manifestations became more extensive, his condition deteriorated rapidly. He bled profusely for 72 hours and then expired.

His initial blood count was normal; however, the count made when his dose of oxytetracycline was increased to 2 Gm. daily was 21,000 white blood cells with 91 per cent polys. The count had fallen to 10,000 white blood cells when the dosage was reduced, but the count was not repeated until the bleeding became evident. With the onset of purpura, his platelet count was 15,000 per cubic millimeter and it remained at this level until he succumbed. The hemoglobin ranged between 9 and 10 g. and the white blood count between 17,000 and 18,000 just prior to his death. There was no evident suppression of any blood elements except the platelets. A bone marrow puncture performed immediately following death was normal except that there was no evidence of platelet production.

The patient had received topical chloramphenicol 3 times for an acute otitis media one week following hospitalization and had also been given caffeine iodide, mersalyl, digitalis, aminophylline, and chloral hydrate during his illness. After reviewing the patient's course and the medications that he had received, the authors concluded that the 26 Gm. of oxytetracycline given over a 22-day period was probably responsible for the thrombocytopenic purpura. Since the septicemia appeared to be well controlled before signs of the purpura developed, they were of the opinion that this factor could be eliminated as a probable cause for the hematologic reaction. R. W.

Acute Pulmonary Infection and Cardiac Failure in Chronic Emphysema. Braun, K., and Izak, G.: Am. Heart J. **49**: 385, 1955.

In seven cases of "chronic spastic bronchitis" and pulmonary emphysema, acute pulmonary infection was found to precipitate congestive heart failure and cyanosis. Treatment consisted of the administration of antibiotics, epinephrine inhalation, and oral or parenteral xanthines. Three patients were given ACTH after the congestive failure had disappeared. Three were digitalized and treated with mercurials. In two instances, short exposures to oxygen inhalation increased acidosis, as shown by mental disturbances, hypoventilation, apnea, and increased plasma CO_2 levels. E. K.